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In reply:—The comparison of doses between species is always difficult, as pointed out by Dr. Selander. Consider, for example, the anticonvulsant doses of phenytoin. In rats, the range is 135 mg/kg (ip) to 2,200 mg/kg (po).* The extrapolated dose in humans is 20–300 times the normal daily recommended oral dose. Most experimental investigators have used local anesthetic doses that would be too large if extrapolated to the human.[1–3] This problem of dosing is common and does not invalidate the study of mechanisms, but rather only implies an expected species difference. Systemic toxic effects were not observed for the local anesthetic doses reported. In studies of topical or local drug administration, concentration and not dose is the most important pharmacologic variable. Using concentrations within the clinical range, the end-point of this and a subsequent study[4] was an insight into the pathogenic mechanisms of nerve injury. It is important to note that the observed pathologic changes were not due to osmotic, *p*H, or vehicle effects, but rather to the actions of the local anesthetics in a concentration-dependent manner. In order to explore these effects, several control solutions were used, including 0.2% NaCl (as in Nesacaine-CE®) and 0.9% NaCl (physiologic saline).

We agree that the power and value of statistical tests are improved by increasing the number of subjects, but the nature of the statistical tables is to make it progressively more difficult to achieve statistical significance for decreasing degrees of freedom. Thus, the ability statistically to discriminate treatment and control groups with small numbers is an indication of a robust effect. Different tests did have different numbers of subjects, as indicated, but this certainly does not invalidate the statistical results.

As stated, horseradish peroxidase studies had been done only with 2-chloroprocaine. Since that time, additional studies have been completed with procaine as well.[4] The results in both cases indicate an increase in permeability of the perineurial barrier, allowing the entrance of horseradish peroxidase tracer into the endoneurium.

Although not discussed in the article, it is not surprising that the areas of the nerve most closely in contact with the highest concentration of anesthetic will be the most affected. A more remote fascicle is probably less likely to be affected by the much diluted anesthetic concentration once the agent has diffused across the tissue space.

Dr. Selander's pioneering work in this field has set the foundation for subsequent studies, and we thank him for bringing attention to questions which must be asked about the clinical relevance of any animal study.

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Central Venous Cannulation: A New and Efficient Device

To the Editor:—Cannulation of the central venous system by the Seldinger technique[1] has become an increasingly important part of invasive monitoring in anesthesia. We have developed and tested a new piece of equipment that may improve on guide wire techniques currently in use. The new device consists of a thin-walled 18-gauge needle connected to a 5 ml syringe that allows a j-wire to pass through the plunger and into the needle (fig. 1).